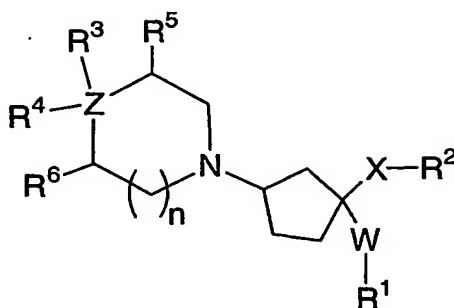


WHAT IS CLAIMED IS:

1. A compound of the formula I:



I

wherein:

X is selected from the group consisting of:

-NR¹⁰-, -O-, -CH₂O-, -CONR¹⁰-, -NR¹⁰CO-, -CO₂-, -OCO-,
-CH₂(NR¹⁰)CO-, -N(COR¹⁰)-, -CH₂N(COR¹⁰)-, phenyl, and
C₃-6 cycloalkyl,

where R¹⁰ is independently selected from: hydrogen, C₁-6 alkyl, benzyl,
phenyl, and C₁-6 alkyl-C₃-6 cycloalkyl,

which is unsubstituted or substituted with 1-3 substituents where the
substituents are independently selected from: halo, C₁-3 alkyl,
C₁-3alkoxy and trifluoromethyl;

W is selected from:

phenyl and heterocycle, which is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from:
halo, C₁-3alkoxy and trifluoromethyl;

Z is selected from:

C, N, and -O-, wherein when Z is N, then R⁴ is absent, and when W is -O-,
then both R³ and R⁴ are absent;

n is an integer selected from 0, 1, 2, 3 and 4;

R¹ is selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- 5 (d) hydroxy,
- (e) C₁-6alkyl,
- (f) C₃-7cycloalkyl,
- (g) -O-C₁-6alkyl,
- (h) -O-C₃-7cycloalkyl,
- 10 (i) -SCF₃,
- (j) -S-C₁-6alkyl,
- (k) -SO₂-C₁-6alkyl,
- (l) phenyl,
- (m) heterocycle,
- 15 (n) -CO₂R⁹,
- (o) -CN,
- (p) -NR⁹R¹⁰,
- (q) -NR⁹-SO₂-R¹⁰,
- (r) -SO₂-NR⁹R¹⁰, and
- 20 (s) -CONR⁹R¹⁰
- (t) -NHC(=NH)NH₂, and
- (u) hydrogen,

R² is selected from:

- 25 (C₀-6alkyl)-phenyl and (C₀-6alkyl)-heterocycle,

where the alkyl is unsubstituted or substituted with 1-7 substituents

where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- 30 (c) -O-C₁-3alkyl,
- (d) trifluoromethyl, and
- (e) -C₁-3alkyl,

and where the phenyl and the heterocycle is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- 5 (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₆alkyl,
- (f) C₃₋₇cycloalkyl,
- 10 (g) -O-C₁₋₆alkyl,
- (h) -O-C₃₋₇cycloalkyl,
- (i) -SCF₃,
- (j) -S-C₁₋₆alkyl,
- (k) -SO₂-C₁₋₆alkyl,
- 15 (l) phenyl,
- (m) heterocycle,
- (n) -CO₂R⁹,
- (o) -CN,
- (p) -NR⁹R¹⁰,
- 20 (q) -NR⁹-SO₂-R¹⁰,
- (r) -SO₂-NR⁹R¹⁰, and
- (s) -CONR⁹R¹⁰;

R³ is -(C₀₋₆alkyl)-phenyl,

25 where the alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- 30 (d) trifluoromethyl,

and where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,

- 5
- (c) hydroxy,
 - (d) C₁₋₃alkyl,
 - (e) -O-C₁₋₃alkyl,
 - (f) -CO₂R⁹,
 - (g) -CN,
 - (h) -NR⁹R¹⁰, and
 - (i) -CONR⁹R¹⁰;

R⁴ is selected from:

- 10
- (a) hydrogen,
 - (b) hydroxy,
 - (c) C₁₋₆alkyl,
 - (d) C₁₋₆alkyl-hydroxy,
 - (e) -O-C₁₋₃alkyl,
 - 15 (f) -CO₂R⁹,
 - (g) -CONR⁹R¹⁰, and
 - (h) -CN;

or where R³ and R⁴ may be joined together to form a ring which is selected from:

- 20
- (a) 1H-indene,
 - (b) 2,3-dihydro-1H-indene,
 - (c) 2,3-dihydro-benzofuran,
 - (d) 1,3-dihydro-isobenzofuran,
 - (e) 2,3-dihydro-benzothiofuran, and
 - 25 (f) 1,3-dihydro-isobenzothiofuran,

or where R³ and R⁵ or R⁴ and R⁶ may be joined together to form a ring which is phenyl,

wherein the ring is unsubstituted or substituted with 1-7 substituents where the substituents are independently selected from:

- 30
- (a) halo,
 - (b) trifluoromethyl,
 - (c) hydroxy,
 - (d) C₁₋₃alkyl,
 - (e) -O-C₁₋₃alkyl,
 - 35 (f) -CO₂R⁹,

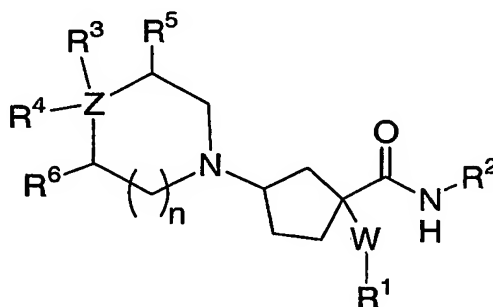
- (g) -CN,
- (h) -NR⁹R¹⁰, and
- (i) -CONR⁹R¹⁰;

5 R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) C₁-6alkyl,
- (d) C₁-6alkyl-hydroxy,
- 10 (e) -O-C₁-3alkyl,
- (f) oxo, and
- (g) halo;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

15 2. The compound of Claim 1 of the formula Ia:

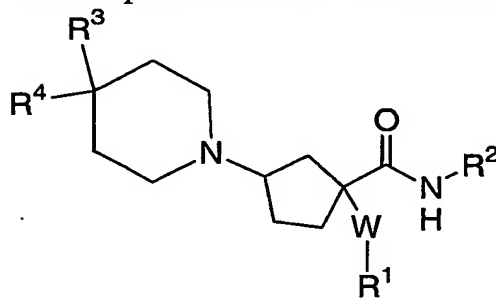


Ia

and pharmaceutically acceptable salts and individual diastereomers thereof.

20

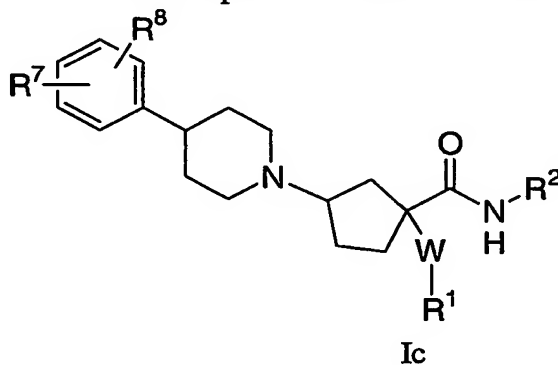
3. The compound of Claim 1 of the formula Ib:



Ib

and pharmaceutically acceptable salts and individual diastereomers thereof.

4. The compound of Claim 1 of the formula Ic:

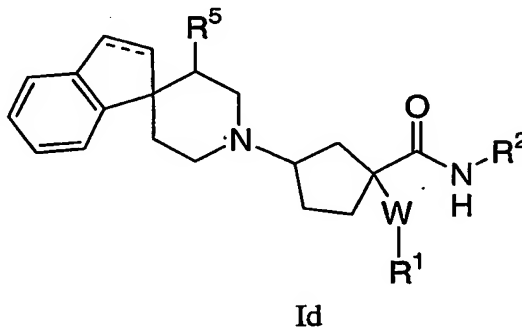


and wherein R⁷ and R⁸ are independently selected from:

- (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂H,
- (h) -CO₂C₁₋₃alkyl, and
- (i) -CN;

and pharmaceutically acceptable salts and individual diastereomers thereof.

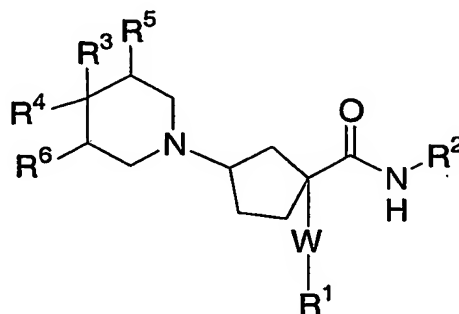
5. The compound of Claim 1 of the formula Id:



wherein the dash line represents either single or double bonds;

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. The compound of Claim 1 of the formula:



5

wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, and thiazolyl, and pharmaceutically acceptable salts and individual diastereomers thereof.

10

7. The compound of Claim 1 wherein W is selected from furanyl, imidazolyl, oxadiazolyl, oxazolyl, phenyl, pyrazolyl, pyrazinyl, pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl, and triazolyl, and N-oxides thereof.

15

8. The compound of Claim 1 wherein X is -CONH-.

9. The compound of Claim 1 wherein Z is -C-, -N- or -O-.

20

10. The compound of Claim 1 wherein n is 0 and 1.

11. The compound of Claim 1 wherein R¹ is selected from:

- (a) hydrogen
- (b) halo
- (c) C₁-3alkyl,
- (d) -O-C₁-3alkyl,
- (e) -CO₂R⁹,
- (f) -S-C₁-3alkyl,
- (g) -SO₂-C₁-3alkyl,

25

- (h) -SCF₃,
- (i) NHC(=NH)NR⁹R¹⁰
- (j) -NR⁹R¹⁰,
- (k) -NR⁹-SO₂-R¹⁰,
- (l) -SO₂-NR⁹R¹⁰, and
- (m) -CONR⁹R¹⁰.

12. The compound of Claim 1 wherein R² is selected from
 -(C₀₋₄alkyl)-phenyl and -(C₀₋₄alkyl)-heterocycle,

where heterocycle is selected from:

furanyl, imidazolyl, oxadiazolyl, oxazolyl, pyrazolyl, pyrazinyl,
 pyridyl, pyridazinyl, pyrimidyl, pyrrolyl, thiadiazolyl, thiazolyl, thienyl,
 and triazolyl, and N-oxides thereof,

where the alkyl is unsubstituted or substituted with 1-7 substituents where the
 substituents are independently selected from:

- (a) halo,
- (b) hydroxy,
- (c) -O-C₁₋₃alkyl, and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-5
 substituents where the substituents are independently selected from:

- (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -CO₂R⁹,
- (h) -S-C₁₋₃alkyl,
- (i) -SO₂-C₁₋₃alkyl,
- (j) -SCF₃,
- (k) -CO₂R⁹,
- (l) -NR⁹R¹⁰,
- (m) -NR⁹-SO₂-R¹⁰,

- (n) $-\text{SO}_2\text{-NR}^9\text{R}^{10}$, and
- (o) $-\text{CONR}^9\text{R}^{10}$.

13. The compound of Claim 1 wherein R^2 is selected from
5 $-(\text{C}_{0-4}\text{alkyl})\text{-phenyl}$ and $-(\text{C}_{0-4}\text{alkyl})\text{-heterocycle}$,
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,
where the alkyl is unsubstituted or substituted with 1-7 substituents where the
substituents are independently selected from:

- (a) halo,
- 10 (b) hydroxy,
- (c) $-\text{O-C}_{1-3}\text{alkyl}$, and
- (d) trifluoromethyl,

and where the phenyl or heterocycle is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from:

- 15 (a) halo,
- (b) trifluoromethyl,
- (c) trifluoromethoxy,
- (d) hydroxy,
- (e) $\text{C}_{1-3}\text{alkyl}$,
- 20 (f) $-\text{O-C}_{1-3}\text{alkyl}$,
- (g) $-\text{CO}_2\text{-C}_{1-3}\text{alkyl}$,
- (h) $-\text{CO}_2\text{H}$,
- (i) $-\text{S-C}_{1-3}\text{alkyl}$,
- (j) $-\text{SO}_2\text{-C}_{1-3}\text{alkyl}$,
- 25 (k) $-\text{SCF}_3$,
- (l) $-\text{NH}_2$,
- (m) $-\text{NH-SO}_2\text{-C}_{1-3}\text{alkyl}$, and
- (n) $-\text{SO}_2\text{-NH}_2$.

30 14. The compound of Claim 1 wherein R^2 is selected from
 $-\text{CH}_2\text{-phenyl}$ and $-\text{CH}_2\text{-heterocycle}$,
where heterocycle is selected from: pyridyl, pyridazinyl, and N-oxides thereof,
and where the phenyl or heterocycle is unsubstituted or substituted with 1-3
substituents where the substituents are independently selected from:

- 5
- (a) halo,
 (b) trifluoromethyl,
 (c) trifluoromethoxy,
 (d) hydroxy,
 (e) C₁₋₃alkyl,
 (f) -O-C₁₋₃alkyl,
 (g) -CO₂-C₁₋₃alkyl,
 (h) -CO₂H,
 (i) -S-C₁₋₃alkyl,
 10 (j) -SO₂-C₁₋₃alkyl,
 (k) -SCF₃,
 (l) -NH₂,
 (m) -NH-SO₂-C₁₋₃alkyl, and
 (n) -SO₂-NH₂.

15

15. The compound of Claim 1 wherein R² is selected from:

- (1) -CH₂-(phenyl),
 (2) -CH₂-(4-bromophenyl),
 (3) -CH₂-(3-chlorophenyl),
 20 (4) -CH₂-(3,5-difluorophenyl),
 (5) -CH₂-((2-trifluoromethyl)phenyl),
 (6) -CH₂-((3-trifluoromethyl)phenyl),
 (7) -CH₂-((4-trifluoromethyl)phenyl),
 (8) -CH₂-((3-trifluoromethoxy)phenyl),
 25 (9) -CH₂-((3-trifluoromethylthio)phenyl),
 (10) -CH₂-((3-trifluoromethoxy-5-thiomethyl)phenyl),
 (11) -CH₂-((3-trifluoromethoxy-5-methoxy)phenyl),
 (12) -CH₂-((3-trifluoromethoxy-5-methanesulfonyl)phenyl),
 (13) -CH₂-((3-trifluoromethoxy-5-amino)phenyl),
 30 (14) -CH₂-((3-trifluoromethoxy-5-aminomethanesulfonyl)phenyl),
 (15) -CH₂-((3-trifluoromethoxy-5-sulfonylamino)phenyl),
 (16) -CH₂-((3,5-bis-trifluoromethyl)phenyl),
 (17) -CH₂-((3-fluoro-5-trifluoromethyl)phenyl),
 (18) -CH(CH₃)-((3,5-bis-trifluoromethyl)phenyl),
 35 (19) -C(CH₃)₂-((3,5-bis-trifluoromethyl)phenyl),

- (20) -CH₂-(4-(2-trifluoromethyl)pyridyl),
(21) -CH₂-(5-(3-trifluoromethyl)pyridyl),
(22) -CH₂-(5-(3-trifluoromethyl)pyridazinyl),
(23) -CH₂-(4-(2-trifluoromethyl)pyridyl-N-oxide), and
5 (24) -CH₂-(5-(3-trifluoromethyl)pyridyl-N-oxide).

16. The compound of Claim 1 wherein R³ is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from:

- 10 (a) halo,
(b) trifluoromethyl,
(c) hydroxy,
(d) C₁-3alkyl,
(e) -O-C₁-3alkyl,
15 (f) -CO₂R⁹,
(g) -CN,
(h) -NR⁹R¹⁰, and
(i) -CONR⁹R¹⁰.

20 17. The compound of Claim 1 wherein R³ is hydrogen or phenyl, where the phenyl is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from:

- (a) halo,
(c) hydroxy,
25 (d) C₁-3alkyl,
(e) -O-C₁-3alkyl, and
(f) -CO₂R⁹.

18. The compound of Claim 1 wherein R³ is phenyl,
30 or para-fluorophenyl.

19. The compound of Claim 1 wherein R⁴ is selected from:

- (a) hydrogen,
(b) hydroxy,

- (c) -CO₂H,
- (d) -CO₂C₁₋₆alkyl,
- (e) -CN.

5 20. The compound of Claim 1 wherein R⁵ and R⁶ are independently selected from:

- (a) hydrogen,
- (b) hydroxy,
- (c) -CH₃,
- 10 (d) -O-CH₃, and
- (e) oxo.

 21. A compound which is selected from the group consisting of the title compounds of the Examples, and pharmaceutically acceptable salts and
15 individual diastereomers thereof.

 22. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

20 23. A method for modulation of chemokine receptor activity in a mammal in need thereof which comprises the administration of an effective amount of the compound of Claim 1.

 24. A method for treating, ameliorating or controlling an
25 inflammatory or immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

 25. A method for reducing the risk of an inflammatory or
30 immunoregulatory disorder or disease which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.

26. A method for treating, ameliorating or controlling rheumatoid arthritis which comprises administering to a patient in need thereof an effective amount of the compound of Claim 1.